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PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

Claim 1 (Currently Amended): A compound, comprising: a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, is a peptide or peptidomimetic, and binds to a receptor that is upregulated during angiogenesis, the receptor is  $\alpha_v \beta_3$ , and the compound has  $\theta$ -1  $\underline{a}$  linking groups between the targeting moiety and chelator, the linking group having the formula:

 $(CR^{6}R^{7})_{g}-(W)_{h}-(CR^{6a}R^{7a})_{g}'-(Z)_{k}-(W)_{h}'-(CR^{8}R^{9})_{g}''-(W)_{h''}-(CR^{8a}R^{9a})_{g''}$ 

wherein,

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>5</sub>, and (aa)<sub>t</sub>;

aa is independently at each occurrence an amino acid;

- Z is selected from the group: aryl substituted with 0-3 R<sup>10</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>10</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>10</sup>;
- R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup> and R<sup>9a</sup> are independently selected at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, PO<sub>3</sub>H, C<sub>1</sub> C<sub>5</sub> alkyl substituted with 0-3 R<sup>10</sup>, aryl substituted with 0-3 R<sup>10</sup>, benzyl substituted with 0-3 R<sup>10</sup>, and C<sub>1</sub> C<sub>5</sub> alkoxy substituted with 0-3 R<sup>10</sup>, NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to the chelator;

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R<sup>10</sup> is independently selected at each occurrence from the group: a bond to the chelator,

COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, aryl substituted with 0-3 R<sup>11</sup>, C<sub>1-5</sub> alkyl

substituted with 0-1 R<sup>12</sup>, C<sub>1-5</sub> alkoxy substituted with 0-1 R<sup>12</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N,

S, and O and substituted with 0-3 R<sup>11</sup>;

R<sup>11</sup> is independently selected at each occurrence from the group: H, aryl substituted with 0-1

R<sup>12</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms
independently selected from N, S, and O and substituted with 0-1 R<sup>12</sup>, C<sub>3-10</sub>

cycloalkyl substituted with 0-1 R<sup>12</sup>, polyalkylene glycol substituted with 01 R<sup>12</sup>,
carbohydrate substituted with 0-1 R<sup>12</sup>, cyclodextrin substituted with 0-1 R<sup>12</sup>, amino
acid substituted with 0-1 R<sup>12</sup>, polycarboxyalkyl substituted with 0-1 R<sup>12</sup>, polyazaalkyl
substituted with 0-1 R<sup>12</sup>, peptide substituted with 0-1 R<sup>12</sup>, wherein the peptide is
comprised of 2-10 amino acids, and a bond to the chelator;

## R<sup>12</sup> is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h" is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; and

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Claim 2 (Currently Amended): A compound according to Claim 1, wherein the targeting moiety is a peptide or a mimetic thereof and the receptor is  $\alpha_{\nu}\beta_{3}$  and the linking group is present between the targeting moiety and chelator.

Claim 3 (Previously Amended): A compound according to Claim 2, the compound is of the formula:

$$(Q)_{d}$$
- $L_{n}$ - $C_{h}$  or  $(Q)_{d}$ - $L_{n}$ - $(C_{h})_{d'}$ 

wherein, Q is a peptide independently selected from the group:

K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylornithine,  $\delta$ -N-benzylcarbamoylornithine, and  $\beta$ -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a-D amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine,  $\delta$ -N-2-imidazolinylornithine,  $\delta$ -N-benzylcarbamoylornithine, and  $\beta$ -2-benzimidazolylacetyl-1, 2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;

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R<sup>1</sup> is an amino acid substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;

R<sup>2</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, valine, alanine, leucine, isoleucine, norleucine, 2 aminobutyric acid, 2-aminohexanoic acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, methionine, and 2-aminothiazole-4-acetic acid;

R<sup>3</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, and D-methionine;

R<sup>4</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, D-methionine, and 2-aminothiazole-4-acetic acid;

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R<sup>5</sup> is an amino acid, substituted with 0-1 bonds to L<sub>n</sub>, independently selected at each occurrence from the group: glycine, L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-serine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine, L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> in each Q is substituted with a bond to L<sub>n</sub>, further provided that when R<sup>2</sup> is 2-aminothiazole-4-acetic acid, K is N-methylarginine, further provided that when R<sup>4</sup> is 2-aminothiazole-4-acetic acid, K and K' are N-methylarginine, and still further provided that when R<sup>5</sup> is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

 $L_n$  is a linking group having the formula:

$$(CR^6R^7)_g$$
- $(W)_h$ - $(CR^{6a}R^{7a})g$ '- $(Z)_k$ - $(W)_h$ '- $(CR^8R^9)_g$ "- $(W)_h$ "- $(CR^{8a}R^{9a})_g$ "

provided that g+h+g'+k+h'+g"+h"+g" is other than 0;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>O)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>, and (aa)<sub>t</sub>;

aa is independently at each occurrence an amino acid;

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- Z is selected from the group: aryl substituted with 0-3 R<sup>10</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>10</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>10</sup>;
- $R^6$ ,  $R^{6a}$ ,  $R^7$ ,  $R^{7a}$ ,  $R^8$ ,  $R^{8a}$ ,  $R^9$  and  $R^{9a}$  are independently selected at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, PO<sub>3</sub>H, C<sub>1</sub> C<sub>5</sub> alkyl substituted with 0-3  $R^{10}$ , aryl substituted with 0-3  $R^{10}$ , benzyl substituted with 0-3  $R^{10}$ , and C<sub>1</sub> C<sub>5</sub> alkoxy substituted with 0-3  $R^{10}$ , NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to C<sub>h</sub>;
- R<sup>10</sup> is independently selected at each occurrence from the group: a bond to C<sub>h</sub>, COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, PO<sub>3</sub>H, aryl substituted with 0-3 R<sup>11</sup>, C<sub>1-5</sub> alkyl substituted with 0-1 R<sup>12</sup>, C<sub>1-5</sub> alkoxy substituted with 0-1 R<sup>12</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>11</sup>;
- R<sup>11</sup> is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R<sup>12</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>12</sup>, C <sub>3-10</sub> cycloalkyl substituted with 0-1 R<sup>12</sup>, polyalkylene glycol substituted with 01 R<sup>12</sup>, carbohydrate substituted with 0-1 R<sup>12</sup>, cyclodextrin substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, polycarboxyalkyl substituted with 0-1 R<sup>12</sup>, polyazaalkyl substituted with 0-1 R<sup>12</sup>, peptide substituted with 0-1 R<sup>12</sup>, wherein the peptide is comprised of 2-10 amino acids, and a bond to C<sub>h</sub>;

R<sup>12</sup> is a bond to C<sub>h</sub>;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h" is selected from 0, 1, 2, 3, 4, and 5;

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g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; g" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; g"' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10; t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

Ch is a metal bonding unit having a formula selected from the group:

 $A^{1}$ ,  $A^{1}$  E  $A^{2}$   $A^{2}$   $A^{3}$   $A^{4}$ ,  $A^{5}$  E  $A^{5}$  E  $A^{6}$  E  $A^{7}$   $A^{1}$   $A^{1}$   $A^{2}$   $A^{2}$   $A^{3}$   $A^{4}$   $A^{5}$   $A^{5}$   $A^{1}$   $A^{2}$   $A^{5}$   $A^{1}$   $A^{2}$   $A^{2}$   $A^{3}$   $A^{4}$   $A^{5}$   $A^{5}$   $A^{1}$   $A^{2}$   $A^{4}$   $A^{5}$   $A^{1}$   $A^{2}$   $A^{4}$   $A^{5}$   $A^{5}$   $A^{1}$   $A^{1}$   $A^{2}$   $A^{2}$   $A^{3}$   $A^{4}$   $A^{5}$   $A^{5}$   $A^{1}$   $A^{1}$   $A^{2}$   $A^{2}$   $A^{3}$   $A^{4}$   $A^{5}$   $A^{5}$ 

 $A^1$ ,  $A^2$ ,  $A^3$ ,  $A^4$ ,  $A^5$ ,  $A^6$ ,  $A^7$ , and  $A^8$  are independently selected at each occurrence from the group N, NR<sup>13</sup>, NR<sup>13</sup>R<sup>14</sup>, S, SH, S(Pg), O, OH, PR<sup>13</sup>, PR<sup>13</sup>R<sup>14</sup>, P(O)R<sup>15</sup>R<sup>16</sup>, and a bond to L<sub>n</sub>;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group:  $C_1$ - $C_{10}$  alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>,  $C_{3-10}$  cycloalkyl

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substituted with 0-3  $R^{17}$ , heterocyclo  $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O,  $C_{6\,10}$  aryl  $C_{1\,10}$  alkyl substituted with 0-3  $R^{17}$ ,  $C_{1\,10}$  alkyl  $C_{6\,10}$  aryl substituted with 0-3  $R^{17}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{17}$ ;

 $R^{13}$ , and  $R^{14}$  are each independently selected from the group: a bond to  $L_n$ , hydrogen,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  cycloalkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O,  $C_{6-10}$  aryl  $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  alkyl  $C_{6-10}$  aryl substituted with 0-3  $R^{17}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{17}$ , and an electron, provided that when one of  $R^{13}$  or  $R^{14}$  is an electron, then the other is also an electron;

alternatively,  $R^{13}$  and  $R^{14}$  combine to form = $C(R^{20})(R^{21})$ ;

 $R^{15}$  and  $R^{16}$  are each independently selected from the group: a bond to  $L_n$ , OH,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ ,  $C_{3-10}$  cycloalkyl substituted with 0-3  $R^{17}$ , heterocyclo  $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O,  $C_{6-10}$  aryl  $C_{1-10}$  alkyl substituted with 0-3  $R^{17}$ ,  $C_{1-10}$  alkyl  $C_{6-10}$  aryl substituted with 0-3  $R^{17}$ , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{17}$ ;

 $R^{17}$  is independently selected at each occurrence from the group: a bond to  $L_n$ , =0, F, Cl, Br, I, -CF<sub>3</sub>, -CN, -CO<sub>2</sub>R<sup>18</sup>, -C(=O)R<sup>18</sup>, -C(=O)N(R<sup>18</sup>)<sub>2</sub>, -CHO, -CH<sub>2</sub>OR<sup>18</sup>, -OC(=O)R<sup>18</sup>, -OC(=O)OR<sup>18a</sup>, -OC(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19C</sup>(=O)R<sup>18</sup>, -NR<sup>19C</sup>(=O)OR<sup>18a</sup>, Page 9 of 31

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-NR<sup>19</sup>C(=O)N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -NR<sup>19</sup>SO<sub>2</sub>R<sup>18a</sup>, -SO<sub>3</sub>H, -SO<sub>2</sub>R<sup>18a</sup>, -SR<sup>18</sup>, -S(=O)R<sup>18a</sup>, -SO<sub>2</sub>N(R<sup>18</sup>)<sub>2</sub>, -N(R<sup>18</sup>)<sub>2</sub>, -NHC(=S)NHR<sup>18</sup>, =NOR<sup>18</sup>, NO<sub>2</sub>, -C(=O)NHOR<sup>18</sup>, -C(=O)NHNR<sup>18</sup>R<sup>18a</sup>, -OCH<sub>2</sub>CO<sub>2</sub>H, 2-(1 morpholino)ethoxy, C<sub>1</sub>-C<sub>5</sub> alkyl, C<sub>2</sub>-C<sub>4</sub> alkenyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkylmethyl, C<sub>2</sub>-C<sub>6</sub> alkoxyalkyl, aryl substituted with 0-2 R<sup>18</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;



 $R^{18}$ ,  $R^{18a}$ , and  $R^{19}$  are independently selected at each occurrence from the group: a bond to  $L_n$ , H,  $C_1$ - $C_6$  alkyl, phenyl, benzyl,  $C_1$ - $C_6$  alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

 $R^{20}$  and  $R^{21}$  are independently selected from the group: H,  $C_1$ - $C_{10}$  alkyl, -CN, -CO<sub>2</sub> $R^{25}$ , -C(=O) $R^{25}$ , -C(=O) $R^{25}$ , -C(=O) $R^{25}$ )<sub>2</sub>,  $C_2$ - $C_{10}$  1-alkene substituted with 0-3  $R^{23}$ , C2-C10 1-alkyne substituted with 0-3  $R^{23}$ , aryl substituted with 0-3  $R^{23}$ , unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{23}$ , and unsaturated  $C_{3-10}$  carbocycle substituted with 0-3  $R^{23}$ ;

alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the divalent carbon radical to which they are attached form:

$$R^{22}$$

$$R^{23}$$

$$R^{23}$$

$$R^{23}$$

$$R^{23}$$

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 $R^{22}$  and  $R^{23}$  are independently selected from the group: H,  $R^{24}$ ,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{24}$ ,  $C_2$ - $C_{10}$  alkenyl substituted with 0-3  $R^{24}$ , and Substituted with 0-3  $R^{24}$ , are substituted with 0-3  $R^{24}$ , and 0-3  $R^{24}$ ;

alternatively, R<sup>22</sup>, R<sup>23</sup> taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and b indicate the positions of optional double bonds and n is 0 or 1;

 $R^{24} \text{ is independently selected at each occurrence from the group: =O, F, Cl, Br, I, -CF_3, -CN, } \\ -CO_2R^{25}, -C(=O)R^{25}, -C(=O)N(R^{25})_2, -N(R^{25})_3+, -CH_2OR^{25}, -OC(=O)R^{25}, \\ -OC(=O)OR^{25a}, -OR^{25}, -OC(=O)N(R^{25})_2, -NR^{26}C(=O)R^{25}, -NR^{26}C(=O)OR^{25a}, \\ -NR^{26}C(=O)N(R^{25})_2, -NR^{26}SO_2N(R^{25})_2, -NR^{26}SO_2R^{25a}, -SO_3H, -SO_2R^{25a}, -SR^{25}, \\ -S(=O)R^{25a}, -SO_2N(R^{25})_2, -N(R^{25})_2, =NOR^{25}, -C(=O)NHOR^{25}, -OCH_2CO_2H, and 2-(1-morpholino)ethoxy; and, \\ \\ \end{array}$ 

 $R^{25}$ ,  $R^{25a}$ , and  $R^{26}$  are each independently selected at each occurrence from the group: hydrogen and  $C_1$ - $C_6$  alkyl;

and a pharmaceutically acceptable salt thereof.

Claim 4 (Currently Amended): A compound according to Claim 3, the present invention provides a compound, wherein:

L is glycine;

R<sup>1</sup> is an amino acid, optionally substituted with a bond to Ln, independently selected at each occurrence from the group: L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, phenylalanine, phenylglycine,

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cyclohexylalanine, homophenylalanine, lysine, ornithine, 1,2-diaminobutyric acid, and 1,2-diaminopropionic acid;

R<sup>2</sup> is an amino acid, optionally substituted with a bond to Ln, independently selected at each occurrence from the group: valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

R<sup>3</sup> is an amino acid, optionally substituted with a bond to Ln, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, and D-1,2-diaminopropionic acid;

R<sup>4</sup> is an amino acid, optionally substituted with a bond to L<sub>n</sub>, independently selected at each occurrence from the group: D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-ornithine, D1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, and 2-aminothiazole4-acetic acid;

R<sup>5</sup> is an amino acid, optionally substituted with a bond to L<sub>n</sub>, independently selected at each occurrence from the group: L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, and 2-aminothiazole-4-acetic acid;

d is selected from 1, 2, and 3;

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W is independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO<sub>2</sub>, (OCH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s</sub>, (OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>s</sub>, and (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>,

Z is selected from the group: aryl substituted with 0-1 R<sup>10</sup>, C<sub>3 10</sub> cycloalkyl substituted with 0-1 R<sup>10</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>10</sup>;

R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup>, and R<sup>9a</sup> are independently selected at each occurrence from the group: H, =O, COOH, SO<sub>3</sub>H, C<sub>1</sub>-C<sub>5</sub> alkyl substituted with 0-1 R<sup>10</sup>, aryl substituted with 0-1 R<sup>10</sup>, benzyl substituted with 0-1 R<sup>10</sup>, and C<sub>1</sub>-C<sub>5</sub> alkoxy substituted with 0-1 R<sup>10</sup>, NHC(=O)R<sup>11</sup>, C(=O)NHR<sup>11</sup>, NHC(=O)NHR<sup>11</sup>, NHR<sup>11</sup>, R<sup>11</sup>, and a bond to C<sub>h</sub>;

R<sup>10</sup> is independently selected at each occurrence from the group: COOR<sup>11</sup>, OH, NHR<sup>11</sup>, SO<sub>3</sub>H, aryl substituted with 0-1 R<sup>11</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>11</sup>, C<sub>1</sub>-C<sub>5</sub> alkyl substituted with 0-1 R<sup>12</sup>, C<sub>1</sub>-C<sub>5</sub> alkoxy substituted with 0-1 R<sup>12</sup>, and a bond to C<sub>h</sub>;

R<sup>11</sup> is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R<sup>12</sup>, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R<sup>12</sup>, polyalkylene glycol substituted with 0-1 R<sup>12</sup>, carbohydrate substituted with 0-1 R<sup>12</sup>, cyclodextrin substituted with 0-1 R<sup>12</sup>, amino acid substituted with 0-1 R<sup>12</sup>, and a bond to C<sub>h</sub>;

k is 0 or 1; h is 0 or 1; h' is 0 or 1; s is selected from 0, 1, 2, 3, 4, and 5; s' is selected from 0, 1, 2, 3, 4, and 5;

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s" is selected from 0, 1, 2, 3, 4, and 5; t is selected from 0, 1, 2, 3, 4, and 5;

 $A^1$ ,  $A^2$ ,  $A^3$ ,  $A^4$ ,  $A^5$ ,  $A^6$ ,  $A^7$ , and  $A^8$  are independently selected at each occurrence from the group:  $NR^{13}$ ,  $NR^{13}R^{14}$ , S, SH, S(Pg), OH, and a bond to  $L_n$ ;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C<sub>1</sub>-C<sub>10</sub> alkyl substituted with 0-3 R<sup>17</sup>, aryl substituted with 0-3 R<sup>17</sup>, C<sub>3-10</sub> cycloalkyl substituted with 0-3 R<sup>17</sup>, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>17</sup>;

 $R^{13}$ , and  $R^{14}$  are each independently selected from the group: a bond to  $L_n$ , hydrogen,  $C_1$ - $C_{10}$  alkyl substituted with 0-3  $R^{17}$ , aryl substituted with 0-3  $R^{17}$ , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3  $R^{17}$ , and an electron, provided that when one of  $R^{13}$  or  $R^{14}$  is an electron, then the other is also an electron;

alternatively,  $R^{13}$  and  $R^{14}$  combine to form = $C(R^{20})(R^{21})$ ;

$$\begin{split} R^{17} \text{ is independently selected at each occurrence from the group: a bond to $L_n$, =0, $F$, $Cl$, $Br$, <math display="block"> I, \quad -CF_3, \quad -CN, \quad -CO_2R^{18}, \quad -C(=O)R^{18}, \quad -C(=O)N(R^{18})_2, \quad -CH_2OR^{18}, \quad -OC(=O)R^{18}, \\ -OC(=O)OR^{18a}, \quad -OR^{18}, \quad -OC(=O)N(R^{18})_2, \quad -NR^{19}C(=O)R^{18}, \quad -NR^{19}C(=O)OR^{18a}, \\ -NR^{19}C(=O)N(R^{18})_2, \quad -NR^{19}SO_2N(R^{18})_2, \quad -NR^{19}SO_2R^{18a}, \quad -SO_3H, \quad -SO_2R^{18a}, \quad -S(=O)R^{18a}, \\ -SO_2N(R^{18})_2, \quad -N(R^{18})_2, \quad -NHC(=S)NHR^{18}, \quad =NOR^{18}, \quad -C(=O)NHNR^{18}R^{18a}, \quad -OCH_2CO_2H, \text{ and } 2\text{-}(1\text{-morpholino})\text{ethoxy}; \end{split}$$

 $R_{18}$ ,  $R_{18a}$ , and  $R_{19}$  are independently selected at each occurrence from the group: a bond to  $L_n$ , H, and  $C_1$ - $C_6$  alkyl;

 $R^{20}$  and  $R^{21}$  are independently selected from the group: H,  $C_1$ - $C_5$  alkyl, - $CO_2R^{25}$ ,  $C_2$ - $C_5$  1-alkyne substituted with 0-3  $R^{23}$ , aryl Page 14 of 31

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substituted with 0-3 R<sup>23</sup>, and unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R<sup>23</sup>;

alternatively, R<sup>20</sup> and R<sup>21</sup>, taken together with the divalent carbon radical to which they are attached form:

$$R^{22}$$

$$R^{23}$$

$$R^{23}$$

$$R^{23}$$

$$R^{23}$$

R<sup>22</sup> and R<sup>23</sup> are independently selected from the group: H, and R<sup>24</sup>;

alternatively, R<sup>22</sup>, R<sup>23</sup> taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

 $R^{24}$  is independently selected at each occurrence from the group:  $-CO2R^{25}$ ,  $-C(=O)N(R^{25})2$ ,  $-CH_2OR^{25}$ ,  $-OC(=O)R^{25}$ ,  $-OR^{25}$ ,  $-SO_3H$ ,  $-N(R^{25})2$ , and  $-OCH_2CO_2H$ ; and,

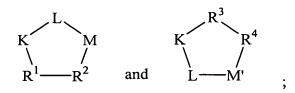
 $R^{25}$  is independently selected at each occurrence from the group: H and  $C_1\text{-}C_3$  alkyl.

Claim 5 (Currently Amended): A compound according to Claim 4, the present invention provides a compound, wherein:

Q is a peptide selected from the group:

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 $R^1$  is L-valine, D-valine, D-lysine optionally substituted on the  $\epsilon$  amino group with a bond to  $L_n$  or L-lysine optionally substituted on the  $\epsilon$  amino group with a bond to  $L_n$ ;

 $R^2$  is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid, L-lysine optionally substituted on the  $\epsilon$  amino group with a bond to  $L_n$  or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to  $L_n$ ;

 $R^3$  is D-valine, D-phenylalanine, or L-lysine optionally substituted on the  $\epsilon$  amino group with a bond to  $L_n$ ;

 $R^4$  is D-phenylalanine, D-tyrosine substituted on the hydroxy group with a bond to  $L_n$ , or L-lysine optionally substituted on the  $\epsilon$  amino group with a bond to  $L_n$ ;

provided that one of  $R^1$  and  $R^2$  in each Q is substituted with a bond to  $L_n$ , and further provided that when  $R^2$  is 2-aminothiazole-4-acetic acid, K is N methylarginine;

d is 1 or 2;

W is independently selected at each occurrence from the group: NHC(=O), C(=O)NH, C(=O), (CH<sub>2</sub>CH<sub>2</sub>O)<sub>s'</sub>, and (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O)<sub>t</sub>;

R<sup>6</sup>, R<sup>6a</sup>, R<sup>7</sup>, R<sup>7a</sup>, R<sup>8</sup>, R<sup>8a</sup>, R<sup>9</sup>, and R<sup>9a</sup> are independently selected at each occurrence from the group: H, NHC(=0)R<sup>11</sup>, and a bond to C<sub>h</sub>;

k is 0;

h" is selected from 0, 1, 2, and 3;

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g is selected from 0, 1, 2, 3, 4, and 5; g' is selected from 0, 1, 2, 3, 4, and 5; g" is selected from 0, 1, 2, 3, 4, and 5; g"' is selected from 0, 1, 2, 3, 4, and 5; s' is 1 or 2; t is 1 or 2;



$$A^{1} \stackrel{E}{=} E \stackrel{A^{4}}{=} E \stackrel{A^{6}}{=} E \stackrel{A^{7}}{=} A^{8}$$
is 
$$A^{3} \stackrel{A^{3}}{=} A^{5}$$

 $A^{1}$  is selected from the group: OH, and a bond to  $L_{n}$ ;

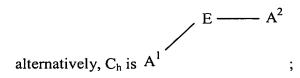
 $A^2$ ,  $A^4$ , and  $A^6$  are each N;

A<sup>3</sup>, A<sup>5</sup>, and A<sup>8</sup> are each OH;

 $A^7$  is a bond to  $L_n$  or NH-bond to  $L_n$ ;

E is a  $C_2$  alkyl substituted with 0-1  $R^{17}$ ;

 $R^{17}$  is =O;



 $A^1$  is  $NH_2$  or  $N=C(R^{20})(R^{21})$ ;

E is a bond;

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A<sup>2</sup> is NHR<sup>13</sup>;

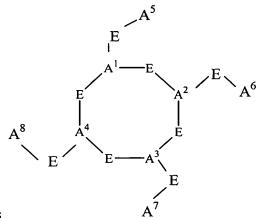
R<sup>13</sup> is a heterocycle substituted with R<sup>17</sup>, the heterocycle being selected from pyridine and pyrimidine;

 $R^{17}$  is selected from a bond to  $L_n$ ,  $C(=O)NHR^{18}$ , and  $C(=O)R^{18}$ ;

 $R^{18}$  is a bond to  $L_n$ ;

 $R^{24}$  is selected from the group:  $CO2R^{25}$ ,  $OR^{25}$ , SO3H, and  $N(R^{25})_2$ ;

R<sup>25</sup> is independently selected at each occurrence from the group: hydrogen and methyl;



alternatively, Ch is

 $A^1$ ,  $A^2$ ,  $A^3$ , and  $A^4$  are each N;

 $A^5$ ,  $A^6$ , and  $A^8$  are each OH;

 $A^7$  is a bond to  $L_n$ ;

E is a C<sub>2</sub> alkyl substituted with 0-1 R<sup>17</sup>; and,

 $R^{17}$  is =0.

- Claim 6 (Currently Amended): A compound according to Claim 3, the present invention provides a compound selected from the group:
- (a) cyclo {Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};



- (b) cyclo {Arg-Gly-Asp-D-Tyr((N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-18-amino-14-aza-4,7,10-oxy-15-oxo-octadecoyl)-3-aminopropyl)-Val};
- (c) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo {D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp})-cyclo {D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp};
- (d) cyclo(Arg-Gly-Asp-D-Tyr-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (e) cyclo {Arg-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (f) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};
- (g) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Phe-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe};
- (h) cyclo {Arg-Gly-Asp-D-Nal-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};

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- (i) [2-[[[5-[carbonyl]-2-pyridinyl]-hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{Lys-Arg-Gly-Asp-D-Nal})-cyclo{Lys-Arg-Gly-Asp-D-Nal};
- (j) cyclo {Arg-Gly-Asp-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Val};
- (k) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{Lys-D-Val-Arg-Gly-Asp})-cyclo{Lys-D-Val-Arg-Gly-Asp};
- (l) {cyclo(Arg-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
- (m) cyclo {D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Phe-D-Asp-Gly-Arg};
- (n) [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{D-Lys-D-Phe-D-Asp-Gly-Arg});
- (o) cyclo {D-Phe-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Asp-Gly-Arg};
- (q) cyclo {Cit-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (r) 2-(1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)-1-cyclododecyl)acetyl-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe};



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- (s) cyclo {Arg-Gly-Asp-D-Phe-Lys(DTPA)};
- (t) cyclo {Arg-Gly-Asp-D-Phe-Lys}2(DTPA);
- (u) Cyclo {Arg-Gly-Asp-D-Tyr(N-DTPA-3-aminopropyl)-Val};
- (v) cyclo {Orn(d-N-2-Imidazolinyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (w) cyclo {Lys-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (x) cyclo {Cys(2-aminoethyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (y) cyclo {HomoLys-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (z) cyclo {Orn(d-N-Benzylcarbamoyl)-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (aa) cyclo {Dap(b-(2-benzimidazolylacetyl))-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-Val};
- (bb) cyclo {Orn(d-N-2-Imidazolinyl)-Gly-Asp-D-Phe-Lys(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};
- (cc) cyclo {Orn(d-N-Benzylcarbamoyl)-Gly-Asp-D-Phe-Lys(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])};



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- (dd) cyclo {Lys-D-Val-D-Tyr(N-[2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};
- (ee) cyclo {Orn(d-N-Benzylcarbamoyl)-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly}; and,
- (ff) cyclo {Orn(d-N-2-Imidazolinyl)-D-Val-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-3-aminopropyl)-D-Asp-Gly};

or a pharmaceutically acceptable salt form thereof.

Claim 7 (Original): A kit comprising a compound of Claim 3, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

Claim 8 (Original): A kit according to Claim 7, wherein the kit further comprises one or more ancillary ligands and a reducing agent.

Claim 9 (Original): A kit according to Claim 8, wherein the ancillary ligands are tricine and TPPTS.

Claim 10 (Original): A kit according to Claim 9, wherein the reducing agent is tin(II).

Claim 11 (Canceled)

Claim 12 (Currently Amended): A composition according to Claim 11

metallopharmaceutical comprising the compound of Claim 1 and, wherein the

metallopharmaceutical is a diagnostic radiopharmaceutical, the metal is a radioisotope
selected from the group: <sup>99m</sup>Tc, <sup>95</sup>Tc, <sup>111</sup>In, <sup>62</sup>Cu, <sup>64</sup>Cu, <sup>67</sup>Ga, and <sup>68</sup>Ga, wherein the
targeting moiety is a peptide or a mimetic thereof and the linking group is present
between the targeting moiety and chelator.

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- Claim 13 (Currently Amended): A composition metallopharmaceutical according to Claim 12, wherein the targeting moiety is a cyclic pentapeptide.
- Claim 14. (Currently Amended): A composition metallopharmaceutical according to Claim 13, wherein the radioisotope is <sup>99m</sup>Tc or <sup>95</sup>Tc, and the radiopharmaceutical metallopharmaceutical further comprises a first ancillary ligand and a second ancillary ligand capable of stabilizing the radiopharmaceutical metallopharmaceutical.
- Claim 15 (Currently Amended): A eomposition metallopharmaceutical according to Claim 14, wherein the radioisotope is <sup>99m</sup>Tc.

Claim 16 (Currently Amended): A composition metallopharmaceutical according to Claim 15, wherein the radiopharmaceutical metallopharmaceutical is selected from the group:

- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(Arg-Gly-Asp-D-Tyr(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-Val));
- <sup>99m</sup>Tc(tricine)(TPPMS)(cyclo(Arg-D-Val-D-Tyr(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-D-Asp-Gly));
- <sup>99m</sup>Tc(tricine)(TPPDS)(cyclo(Arg-D-Val-D-Tyr(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-D-Asp-Gly));
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(Arg-D-Val-D-Tyr(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-D-Asp-Gly));
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(Arg-Gly-Asp-D-Phe-Lys(N-[[5-[carbonyl]-2-pyridinyl]diazenido])));

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- 99mTc(tricine)(TPPTS)(cyclo(Arg-Gly-Asp-D-Tyr-Lys(N-[[5-[carbonyl]-2-pyridinyl]diazenido])));
- <sup>99m</sup>Tc(tricine)(TPPTS)([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Phe-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe});
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo {Arg-Gly-Asp-D-Nal-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])});
- <sup>99m</sup>Tc(tricine)(TPPTS)([2-[[[5-[carbonyl]-2-pyridinyl]-hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{Lys-Arg-Gly-Asp-D-Nal})-cyclo{Lys-Arg-Gly-Asp-D-Nal});
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(Arg-Gly-Asp-D-Tyr((N-[[5-[carbonyl]-2-pyridinyl]diazenido]-18-amino-14-aza-4,7,10-oxy-15-oxo-octadecoyl)-3-aminopropyl)-Val));
- <sup>99m</sup>Tc(tricine)(TPPTS)(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu(O-cyclo(Lys-Arg-Gly-Asp-D-Phe))-O-cyclo(Lys-Arg-Gly-Asp-D-Phe));
- <sup>99m</sup>Tc(tricine)(TPPTS)(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-Glu(O-cyclo(D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp))-O-cyclo(D-Tyr(3-aminopropyl)-Val-Arg-Gly-Asp));
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(Arg-Gly-Asp-Lys(N-[[5-[carbonyl]-2-pyridinyl]diazenido])-D-Val));
- <sup>99m</sup>Tc(tricine)(TPPTS)(cyclo {D-Lys([2-[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Phe-D-Asp-Gly-Arg});
- <sup>99m</sup>Tc(tricine)(TPPTS)([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo {D-Lys-D-Phe-D-Asp-Gly-Arg})-cyclo {D-Lys-D-Phe-D-Asp-Gly-Arg});

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<sup>99m</sup>Tc(tricine)(TPPTS)(cyclo {D-Phe-D-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])-D-Asp-Gly-Arg});

<sup>99m</sup>Tc(tricine)(TPPTS)(cyclo(N-Me-Arg-Gly-Asp-ATA-D-Lys(N-[[5-[carbonyl]-2-pyridinyl]diazenido])));

<sup>99m</sup>Tc(tricine)(TPPTS)(cyclo{Cit-Gly-Asp-D-Phe-Lys([2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid])}); and,

<sup>99m</sup>Tc(tricine)(1,2,4-triazole)(cyclo(Arg-Gly-Asp-D-Tyr(N-[[5-[carbonyl]-2-pyridinyl]diazenido]-3-aminopropyl)-Val)).

Claim 17 (Currently Amended): A composition metallopharmaceutical according to Claim 13, wherein the radioisotope is <sup>111</sup>In.

Claim 18 (Currently Amended): A composition metallopharmaceutical according to Claim 17, wherein the radiopharmaceutical metallopharmaceutical is selected from the group:

(DOTA-<sup>111</sup>In)-Glu(cyclo {Lys-Arg-Gly-Asp-D-Phe})-cyclo {Lys-Arg-Gly-Asp-D-Phe}; cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA-<sup>111</sup>In)); and,

cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA-111In).

Claim 19 (Currently Amended): A composition according to Claim 11

metallopharmaceutical comprising the compound of Claim 1 and, wherein the

metallopharmaceutical is a therapeutic radiopharmaceutical, the metal is a

radioisotope selected from the group: <sup>186</sup>Re, <sup>188</sup>Re, <sup>153</sup>Sm, <sup>166</sup>Ho, <sup>177</sup>Lu, <sup>149</sup>Pm, <sup>90</sup>Y,

<sup>212</sup>Bi, <sup>103</sup>Pd, <sup>109</sup>Pd, <sup>159</sup>Gd, <sup>140</sup>La, <sup>198</sup>Au, <sup>199</sup>Au, <sup>169</sup>Yb, <sup>175</sup>Yb, <sup>165</sup>Dy, <sup>166</sup>Dy, <sup>67</sup>Cu, <sup>105</sup>Rh,

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<sup>111</sup>Ag, and <sup>192</sup>Ir, the targeting moiety is a peptide or a mimetic thereof and the linking group is present between the targeting moiety and chelator.

Claim 20 (Currently Amended): A composition metallopharmaceutical according to Claim 19, wherein the targeting moiety is a cyclic pentapeptide.

Claim 21 (Currently Amended): A composition metallopharmaceutical according to Claim 20, wherein the radioisotope is <sup>153</sup>Sm.

Claim 22 (Currently Amended): A composition metallopharmaceutical according to Claim 21, wherein the radiopharmaceutical metallopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA-153Sm));

cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA-153Sm); and,

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(153Sm)-3-aminopropyl)-Val).

Claim 23 (Currently Amended): A composition metallopharmaceutical according to Claim 20, wherein the radioisotope is <sup>177</sup>Lu.

Claim 24 (Currently Amended): A composition metallopharmaceutical according to Claim 23, wherein the radiopharmaceutical metallopharmaceutical is selected from the group:

cyclo(Arg-Gly-Asp-D-Phe-Lys(DTPA-177Lu));

 $(DOTA-^{177}Lu)-Glu(cyclo\{Lys-Arg-Gly-Asp-D-Phe\})-cyclo\{Lys-Arg-Gly-Asp-D-Phe\};\\$ 

cyclo(Arg-Gly-Asp-D-Phe-Lys)2(DTPA-<sup>177</sup>Lu); and, Page 26 of 31

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cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(177Lu)-3-aminopropyl)-Val).

Claim 25 (Currently Amended): A composition metallopharmaceutical according to Claim 20, wherein the radioisotope is <sup>90</sup>Y.

Claim 26 (Currently Amended): A composition metallopharmaceutical according to Claim 25, wherein the radiopharmaceutical metallopharmaceutical is:

 $(DOTA-^{90}Y)-Glu(cyclo\{Lys-Arg-Gly-Asp-D-Phe\})-cyclo\{Lys-Arg-Gly-Asp-D-Phe\};$ 

Claim 27 (Currently Amended): A composition according to Claim 11

metallopharmaceutical comprising the compound of Claim 1 and, wherein the metallopharmaceutical is a MRI contrast agent, the metal is a paramagnetic metal ion selected from the group: Gd(III), Dy(III), Fe(III), and Mn(II), wherein the targeting moiety is a peptide or a mimetic and the linking group is present between the targeting moiety and chelator.

Claim 28 (Currently Amended): A composition metallopharmaceutical according to Claim 27, wherein the targeting moiety is a cyclic pentapeptide.

Claim 29 (Currently Amended): A composition metallopharmaceutical according to Claim 28, wherein the metal ion is Gd(III).

Claim 30 (Currently Amended): A composition metallopharmaceutical according to Claim 29, wherein the contrast agent is:

cyclo(Arg-Gly-Asp-D-Tyr(N-DTPA(Gd(III))-3-aminopropyl)-Val).

Claim 31 (Currently Amended): A composition according to Claim 11

metallopharmaceutical comprising the compound of Claim 1 and a, wherein the

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metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, wherein the targeting moiety is a cyclic pentapeptide, and the linking group is present between the targeting moiety and chelator.

- Claim 32 (Currently Amended): A method of treating rheumatoid arthritis in a patient comprising: administering a therapeutic radiopharmaceutical metallopharmaceutical of Claim 11 19 capable of localizing in new angiogenic vasculature to a patient by injection or infusion.
- Claim 33 (Currently Amended): A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical metallopharmaceutical of Claim 11 19 by injection or infusion.
- Claim 34 (Currently Amended): A method of imaging formation of new blood vessels in a patient comprising: (1) administering a metallopharmaceutical comprising the compound of Claim 1 and a metal diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11 to a patient by injection or infusion; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.
- Claim 35 (Currently Amended): A method of imaging cancer in a patient comprising: (1) administering a diagnostic radiopharmaceutical metallopharmaceutical of Claim 12 to a patient by injection or infusion; (2) imaging the patient using planar or SPECT gamma scintigraphy, or positron emission tomography.

Claims 36-47 (Canceled)

Claim 48 (Currently Amended): A therapeutic radiopharmaceutical composition, comprising:

(a) a therapeutic radiopharmaceutical metallopharmaceutical of Claim 11 19; and, Page 28 of 31

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(b) a parenterally acceptable carrier.

Claim 49 (Currently Amended): A diagnostic radiopharmaceutical composition, comprising:

- (a) a metallopharmaceutical comprising the compound of Claim 1 and a metal diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of Claim 11; and,
- (b) a parenterally acceptable carrier.

Claim 50 (Original): A therapeutic radiopharmaceutical composition, comprising: a radiolabelled targeting moiety, wherein the targeting moiety is a compound Q of Claim 3 and the radiolabel is a therapeutic isotope selected from the group: <sup>35</sup>S, <sup>32</sup>P, <sup>125</sup>I, <sup>131</sup>I, and <sup>211</sup>At.

Claim 51 (Canceled)